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STATUS THYMO-LYMPHATICUS AND ITS RELATION TO SUDDEN DEATH.*

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Adults and children with the condition known as status thymo-lymphaticus are especially liable to die from infectious disease, and are particularly subject to death from shock and death from anesthesia.

The term status thymo-lymphaticus, or status lymphaticus, is applied to people who present hyperplasia of the thymus gland, lymph-nodes, tonsils, lymphatic elements of the spleen and intestinal tract, and lymphoid marrow of the long bones. Associated with this condition are often found hypoplasia of the heart and arteries, evidences of infantilism, signs of old or recent rickets, abnormalities of the thyroid gland, idiopathic epilepsy (Ohlmacher), acromegalia, Addison's disease and myxedema. There are many grades of status lymphaticus from cases showing simple hyperplasia of the thymus to those exhibiting extreme enlargement of this gland with pronounced hyperplasia of all the lymphatic elements of the body.

There is considerable doubt that status thymicus and status lymphaticus are identical conditions. Adami and Nicholls state that they personally regard the thymus as a lymphatic organ. According to Hart, the newer investigations of Wiesel and Hedinger tend to prove that the two are essentially different phenomena. In pure status lymphaticus there is present a *hypoplasia* of the chromaffin system, especially in the adrenals, analogous to that found in Addison's disease. In pure thymus hyperplasia, on the contrary, the chromaffin system is always well-developed. Again, the thymus is developmentally an epithelial organ, derived from the hypoblast of the third visceral cleft. The epithelial elements gradually atrophy, the sole representatives of their existence being the Hassall bodies, which are supposed to be due to the coalescence of the epithelial remnants. The structure is finally substituted by vascular connective tissue from which the lymphoid elements are derived (Adami and Nicholls). Thus the thymus at birth consists

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largely of lymphatic tissue like that of the lymph-nodes, spleen and other organs of the lymphatic system.

For the purpose of this paper we shall speak of status thymicus and status lymphaticus as identical, using the terms status lymphaticus or status thymo-lymphaticus synonymously. Perhaps future investigators may throw light on this interesting problem.

NORMAL WEIGHT OF THYMUS. The question as to the normal weight of the thymus at different ages is a much-mooted one. Hammar believes that the thymus undergoes rapid involution in both acute and chronic illnesses. In death from disease, he claims that the organ is often reduced to one-twentieth or more of its normal weight. In support of this view Hammar quotes Johnson, who reports that four days' starvation of dogs diminishes the thymus to two-thirds its normal weight; while thirty days chronic underfeeding brings about a thymus weight of one one-hundredth of the normal. Below are given figures for the normal weight of the thymus at different ages, taken from Hart:

HAMMAR		FRIEDLEBEN.		VON SURY.	
	Grams		Grams		Grams
For new-born	13.26	1- 9 months	20.7	New-born	14.4
1- 5 years	22.98	9-24 "	27.3	Child in 1 month	15.
6-10 "	26.10	2-14 years	27.	2-9 months 2 year	24.3
11-15 "	37.52	15-25 "	22.1	9 months 2 year	23.2
16-20 "	25.58	25-75 "	3.1	2 11 year	25.8
21-25 "	24.73				
26-35 "	19.87				
36-45 "	16.27				
46-55 "	12.85				
56-65 "	16.08				
66-75 "	6.00				

Table of Average Weight of Thymus Gland.

Thus we see that the average weights obtained by Hammar are much greater than those of Friedleben and von Sury. Hammar attributes this to the fact that his material is taken from one hundred and twenty-six individuals who died while in complete health from accidental causes. On the contrary, von Sury's figures, which practically agree with Friedleben's, were taken from children who died from acute and chronic diseases.

According to von Sury and Friedleben the greatest weight of the thymus (27 g.) is attained at the end of the second year; while Hammar's statistics place the maximum weight (37 g.) between the eleventh and fifteenth years. The latter view, which is more probably correct, is substantiated according to Hammar, by observations conducted by Söderlund and Backman. It was found that the height of the thymus curve was reached in dogs at the end of the fourth month of life, at the time when spermatogenesis be-

gins. This period in dogs corresponds to the period of puberty in men (eleven to fifteen years).

In passing, it is interesting to note that Hammar believes the weight of the thymus gland as a whole is no criterion for estimating the amount of parenchyma of the organ, which is the functionating part. For example, at the ages of one to five years an average thymus weight of about twenty-three grams corresponds to a parenchyma of about twenty grams. At the ages of twenty-one to twenty-five years, the average weight of twenty-five grams has a parenchyma of scarcely five grams.

As far back as 1889, Paltauf of Vienna called attention to the fact that status lymphaticus was responsible for sudden death from shock and immersion in cold water, and that the subjects of this condition bore chloroform anesthesia badly. His writings acted as a stimulus to investigations in this field; until now numerous instances are on record. Paltauf reported the case of a twenty-year-old factory worker swimming with his companions in a stream, who suddenly shrieked, sank under water, and was brought up almost immediately a corpse. Autopsy showed a thymus ten centimeters long, one centimeter thick, five to six centimeters broad; contracted aorta, heart fairly large and pale. Lymph-glands and spleen enlarged and pale. Adenoid tissue of naso-pharynx and base of tongue hypertrophied. Paltauf reported a case of Nordmann's somewhat similar to the one just quoted. A twenty-year-old recruit went swimming before his mid-day meal. After a few minutes in the water he returned to the shore, had a chill, and fell to the ground, rolling his eyes. In spite of attempts to resuscitate him, the young man quickly died. Autopsy revealed dark fluid blood, edema of the lungs, congested internal organs, hyperplasia of the thyroid, faucial and lingual tonsils, lymph glands and spleen. The thymus was the size of a man's fist.

During the past year the writer has seen several reports of sudden deaths from the subcutaneous injection of diphtheria antitoxin, where the patients were said to be subjects of status lymphaticus.

Recently there have been a large number of autopsies in New York at the City Morgue, upon workmen who have died of Caisson disease. In many of these status lymphaticus was present. It is highly probable that status lymphaticus increases the liability to sudden death in compressed-air workers.

Sudden Death From Anesthesia. Of great interest to the surgeon is the relation of status lymphaticus to death from

the use of both general and local anesthetics. Blake has reported seven cases, operated upon in Roosevelt Hospital in one year, who died during or shortly after ether necrosis, where the only discoverable cause of death was status lymphaticus. Hart mentions the following fatalities due to status lymphaticus in connection with the use of general anesthesia:

1. Laquer's case, a fourteen-year-old boy operated upon for the enucleation of an eye-ball. 2. Michl's case, three-quarters of an hour chloroform narcosis; ear operation. Patient suddenly became asphyxtic, Cheyne-Stokes respiration, death. 3. Ploc saw a sixteen-year-old boy die suddenly at the beginning of narcosis. 4. Lecêne saw a man thirty-two years old, who, after incision of a bubo under general narcosis, suddenly died while apparently in the best of condition. Weight of thymus, thirty-five grams. 5. Katholicky had a female patient forty-six years old, upon whom a hernicotomy was performed under chloroform narcosis, who died suddenly four days after operation, apparently from heart collapse. Dimensions of thymus 8x7x2 cm. 6. W. J. McCardie collected a series of thirty fatalities. The anesthetic was chloroform 17 times, ether 6 times, a mixture of chloroform and ether 5 times. Two were doubtful cases, the anesthetic being nitrous oxide gas.

7. Under local anesthesia three deaths have been recorded: (a) Horoszkiewicz, quoted by McCardie—Tropocaine, 0.075 gm injected locally for the removal of a small cyst of the neck. (b) T. J. Harris' case of tonsilotomy, cocaine anesthesia. The operation was quickly performed. It was almost immediately followed by syncope and death. The patient was an adult. Autopsy revealed a thymus weighing eighteen grams. (c) H. Nettel's case of a woman thirty-four years old, Schleich's infiltration anesthesia for the removal of an exophthalmic goiter. Autopsy—Status lymphaticus with enormous hyperplasia of the entire lymphatic apparatus. 8. Warthin reported the case of a woman forty-one years old, who died suddenly during anesthesia. Status lymphaticus. Persistent thymus—Cardiac death. Microscopically "lymphoid exhaustion of lymph-nodes and spleen." 9. Roberts records the case of a twenty-three-year-old woman who died three minutes after the administration of two drams of bromide of ethyl for the extraction of a tooth. Autopsy showed status lymphaticus, the thymus measuring 3x2½x⅜ inches. 10. L. M. Hurd performed an adenoid and tonsil operation upon a negro child 2½ years old under ether anesthesia, who was returned to the ward from the oper-

ating room in good condition. The child died suddenly twenty-five minutes after operation. Autopsy demonstrated a large thymus covering the whole anterior surface of the heart and great vessels, also hyperplasia of lymphatic system. The larynx, trachea and bronchi contained no evidence of blood clot.

These reports demonstrate conclusively that chloroform is the most dangerous anesthetic to use if status lymphaticus exists. In adenoid and tonsil operations, especially, chloroform should be avoided.

Notwithstanding the fact that many eminent authorities deny the existence of thymic asthma and thymic death due to mechanical pressure of the enlarged thymus gland upon the trachea; yet this undoubtedly occurs. Jackson reported a case of thymic asthma which well illustrates this type. A boy four years old was brought to him for the relief of dyspnea and stridulous breathing, steadily increasing since an attack of croup six weeks before. Tracheotomy failed to relieve the dyspnea, it being necessary to pass a long bronchoscopic tube to get by the obstruction. By direct inspection the walls of the trachea were seen to be collapsed from before backward. The performance of thymectomy relieved the dyspnea permanently. The enlarged thymus gland was demonstrated by radiography before operation.

In view of the paucity of our knowledge concerning status lymphaticus, the following cases may be of interest. All but one are taken from the Bellevue Hospital Pathological Department Records. I wish to acknowledge my indebtedness to Dr. Charles Norris, the director of this laboratory, for permission to publish the following notes:

CASES OF STATUS LYMPHATICUS.

Case 1. Italian child, seven months old. Brought to New York Post-Graduate Hospital because of dyspnea and cyanosis. Second day of illness began to cough, and breathing became labored. Nurse in attendance suspected foreign body in air passages from actions of child. Third day auscultation revealed a few subcrepitant râles at bases of lungs. Temperature rose, and child died. Autopsy: Broncho-pneumonia; dilatation of the heart; congestion of meninges; cloudy swelling of kidneys and liver; enlargement of inguinal, cervical, axillary, bronchial and mesenteric lymph-nodes. Thymus greatly enlarged. Dimensions: Length, two inches; breadth, two and three-quarter inches; thickness three-quarters

of an inch. Microscopic examination: Simple hyperplasia of thymus.

Case 2. Boy, nine years old. Epidemic cerebro-spinal meningitis. Duration of illness, two days. Status lymphaticus. Thymus enlarged, extending almost to auriculo-ventricular groove. Spleen small. Lymphoid elements prominent. Peyer's patches and lymphoid follicles of intestine hyperplastic. Mesenteric lymph-nodes enlarged to size of almond. Hypertrophy of tonsillar ring.

Case 3. Boy, twelve years old. Ill four and one-half days. Epidemic cerebro-spinal meningitis. Status lymphaticus. No axillary or pubic hair, pubes being covered with lanugo. Thymus enlarged, extending half way down over pericardium. Marked hypertrophy of lingual, pharyngeal and faucial tonsils. Aorta is narrow.

Case 4. Male, aged eighteen years. Epidemic cerebro-spinal meningitis. Patient unconscious when admitted to Bellevue Hospital. Only five days in United States. Large well-developed subject. Lanugo on lips and face. Axillary hair scant. General rotundity of limbs. Thymus enlarged, reaching down to auricles of heart. Hypoplasia of aorta.

Case 5. Male, nineteen years old. Epidemic cerebro-spinal meningitis. Death on fourth day of illness. Status lymphaticus. Suppurative pericarditis. Thymus enlarged, extending downward to pericardium. Pulmonary valve has only two cusps. Retro-peritoneal glands enlarged. No lymphoid hyperplasia of spleen or intestinal tract.

Case 6. Female child, twelve years old. Epidemic cerebro-spinal meningitis; acute mastoiditis; acute parenchymatous nephritis. Status lymphaticus. Death on second day of illness. Thymus enlarged 12x6x1½ cm. Weight thirty-one grams. Pubic hair developed. Axillary hair absent. Well-developed body. Inguinal, axillary and cervical nodes enlarged to size of almonds. Large adenoid. Hypertrophy of faucial tonsils. Aorta shows a dimple of the ductus arteriosus, with a prominent ridge above it, taking in half the circumference of the vessel, which is slightly stenosed. Both adrenals swollen and hemorrhagic, the right measuring 5x3x1 cm. Uterus, 3 cm. long, of which 2 cm. belongs to cervix and 1 cm. to body.

Case 7. Female, twenty-eight years old. Epidemic cerebro-spinal meningitis. Status lymphaticus. Duration of illness twenty-four hours. Persistent thymus, glandular on section. Mesenteric

and retro-peritoneal glands hyperplastic, and as large as almonds. Superficial lymph-nodes and faucial tonsils enlarged.

Case 8. Male, eighteen years old. Pyemia. Death on eleventh day of illness. Status lymphaticus. Thymus enlarged, reaching to lower border of third rib. Staphylococcus isolated from blood during life. Multiple abscesses of lungs, suppurative myelitis Poorly nourished subject; broad perineum. Small external genitals. Pubic hair female type. No axillary hair and none on chest. Bronchial lymph-nodes enlarged and suppurating. Peyer's patches and solitary follicles of small intestine are prominent. Mesenteric and retro-peritoneal glands enlarged.

Case 9. Woman, twenty-three years old. Exophthalmic goiter. Status lymphaticus. No history obtained. Thymus enlarged. Weight thirty grams, completely covers pericardium. Small woman, fairly well developed. Pubic hair well developed. Retro-peritoneal lymph-nodes contain tubercular foci. Lingual and faucial tonsils enlarged. Marked hypertrophy of lymphoid follicles of pharynx. Mesenteric lymph-nodes enlarged. Thyroid and parathyroids enlarged.

Case 10. Boy, five years old. Ill for one week; intubated on suspicion of diphtheric laryngitis. Autopsy, status lymphaticus Larynx normal. Thymus enlarged, weighing thirty-three grams. Peripheral lymph-glands are enlarged to size of large peas or almonds. Hypertrophy of faucial and lingual tonsils. Mesenteric and bronchial glands enlarged, the latter being slightly pigmented. No note made of collapse of walls of trachea. This case resembles the type due to suffocation caused by mechanical compression of trachea by enlarged thymus gland.

PATHOLOGY OF STATUS LYMPHATICUS.

The gross lesions of status lymphaticus found after death consist, as already stated, of hyperplasia of the thymus gland and lymphatic elements throughout the body. The hyperplasia of the thymus is described by Ewing "as usually being a simple hyperplasia of the lymphoid cells, enlarging and multiplying the follicles sometimes causing the deposit of small nodules of lymphoid cells in the centers of the lobules, in the trabeculæ, or even in the outlying adipose tissue." With the general hyperplasia of the lymphoid elements Blumer found a proliferation of the endothelial cells lying along the trabeculæ of the organ. The thymus is occasionally fatty.

The hyperplasia of the lymphatic system is shown by enlargement of the cervical, axillary, inguinal, mesenteric and bronchial lymph-glands, by hyperplasia of the faucial, pharyngeal and lingual tonsils. The solitary and agminated lymph-follicles in the intestinal tract are often hyperplastic, and there is generally present an enlargement of the spleen, due to a similar simple hyperplasia of the lymphoid elements, accompanied by hyperemia. On cross-section the enlarged malpighian bodies of the spleen stand out prominently from the surrounding pulp. There is occasionally an infiltration of the spleenic pulp by the lymphoid cells. Ewing has observed a hyperplasia of the lymphoid marrow of the long bones and McCardie an enlargement of the tongue, in addition to the hypertrophy of the lingual tonsil. I am inclined to think this observation of McCardie an accidental finding, due to some other cause than status lymphaticus. Paltauf noted a lessening in the amount of hemoglobin in the blood, while Ewing in one instance observed a lymphocytosis of seventy-six per cent.

Anomalies of the heart and arteries are frequently present. Case 2 presented a pulmonary valve with but two cusps, while cases 3 and 6 showed hypoplasia of the aorta. This latter lesion produces a small pulse which may be detected clinically.

Anomalies of the thyroid gland are often found in people dying from status lymphaticus. Wynne, quoted by McCardie, reports a series of twenty cases, in all of which the thyroid was abnormal. In ten it was markedly enlarged. In the others it was of normal size, or but slightly enlarged. Microscopic examination showed marked changes in all twenty cases, either reduction or absence of the colloid material, with hyperplasia of the cells which grow into the alveoli. Warthin observed hyperplasia of the parathyroids in one case of status lymphaticus, associated with acromegalia. Among associated conditions, exophthalmic goiter probably ranks first in importance. Capelle, quoted by Hart, states: 1. Among 19 Basedow patients who died of intercurrent diseases, 14 were thymus carriers, i. e., 44 per cent; 2. Among 17 patients who died from Basedow's disease, 14 were thymus carriers, i. e., 82 per cent.

Other associated conditions are idiopathic epilepsy, acromegalia, myxedema, rickets and Addison's disease. Hedinger states that in a strikingly large number of cases he found Addison's disease in combination with status lymphaticus.

From a study of the cases already quoted, we see that status lymphaticus is a frequent cause of sudden death during anesthesia, infectious disease, and from trivial shock, such as bathing, etc. In

the cases of meningitis reported by the writer, death occurred early in the disease, distinctly modifying its course. Daut, quoted by Blumer, states that in a series of patients dying from diphtheria, over 25 per cent had status lymphaticus. He says that "distinct modifications of the clinical picture of the disease (diphtheria) were present in these cases. In some instances the patients had a hoarse barking cough, and a hoarse voice, associated with attacks of spasmodic suffocation, weakness of the heart and rapidity of the pulse. These attacks were altogether out of proportion to the severity of the membrane formation as shown post-mortem. In other cases the patients died suddenly, having shown no unusual symptoms during life referable to status lymphaticus."

THEORIES OF DEATH: There are three theories advanced to account for sudden death in status lymphaticus: 1. Theory of mechanical compression; 2. Paltauf's theory; 3. Theory of hyperthymization.

1. Compression Theory. It has been proven that in rare instances the enlarged thymus gland may compress the trachea sufficiently to cause death by suffocation. The relief afforded by thymectomy is proof of this fact. In this connection the thickness of the thymus is of more importance than its other dimensions, as the following figures of von Sury show:

Average thickness of thymus		Average sterno-vertebral distance
Newly-born	1.1 cm.	1.6 cm.
Child in 1 month	1.4 cm.	1.7 cm.
Child in 2-9 months	1.5 cm.	2.0 cm.

Thus we see that at the superior aperture of the thorax there is normally only a space of one-half cm. between thymus and the bony walls of the chest, measuring from before backward. Forcible extension of the head decreases this distance. In rickets this sterno-vertebral distance is apt to be small, owing to the frequent occurrence of lordosis.

2. Paltauf's Theory. Paltauf believes that the hyperplasia of the thymus and lymphatic apparatus is due to an intoxication of the organism caused by faulty tissue changes, or by such common causes as infection and hereditary syphilis. The nerve centers governing the movements of the heart become affected, and a lessened resistance of the individual toward harmful external influences is induced. Under such circumstances the heart may suddenly become incapable of functionating.

3. Theory of Hyperthymization. There is thought to be a pathological increase of the internal secretion of the hyperplastic

thymus, which renders the organism more susceptible to external influences. According to Hart, Barbarossa states that thymectomized animals are capable of offering considerable resistance to chloroform poisoning, while animals and men with persistent thymus glands succumb to small amounts of this drug. Further, the theory of hyperthymization is substantiated by the findings in Basedow's disease. Wiesel holds that the hypoplasia of the chromaffin system found in status lymphaticus is responsible for a diminution in the tonicity of the vessel walls and cardiac muscle. Thus sudden death from arterial and cardiac atony and dilatation may occur.

Mode of Death. In the cases of death during anesthesia collected by McCardie, that observer reports that death always occurred suddenly. "In certain cases facial pallor and dilated pupils were first noticed, and then it was found that cardiac action had stopped. In others respiration was observed to become superficial and intermittent, and at the same time the pulse was impalpable; in yet others cyanosis first appeared together with dyspnea, the circulation quickly failing afterwards. In another type of case there was a sudden failure of circulation and respiration, apparently simultaneously." The heart and right ventricle were usually found dilated. The ages of the cases in McCardie's series varied from six months to fifty-five years.

Diagnosis of Status Lymphaticus. It is a deplorable fact that none of the cases of status lymphaticus dying under anesthesia have been diagnosticated before autopsy; yet the diagnosis can undoubtedly be made if the condition is borne in mind, and the patient properly examined. Status lymphaticus should be suspected in an individual who gives a history of one or more sudden unexplained deaths in other members of his family. Hedinger reported the sudden deaths of five children in one family, before they reached the age of six. Autopsy on one of them showed a large thymus and status lymphaticus.

Individuals with status lymphaticus often have a pasty skin, a large amount of subcutaneous fat, and may show evidences of old or recent rickets (Conner). There is a general rotundity of the limbs, which is very characteristic, and which was noted in case 4 of this series. Adults often show an absence or scanty condition of the axillary and pubic hairs, which, together with the hair of the head, may have a peculiar dry, brittle character. In adults signs of infantilism may be present, characterized by small external genitals or an infantile uterus. There is generally an enlargement

of the external lymphatic glands, axillary, cervical and inguinal, accompanied by hyperplasia of the faucial, pharyngeal and lingual tonsils. The spleen may also be enlarged and palpable.

McCardie states that "signs of low blood-pressure may be associated, e. g., pupils comparatively large, a low tension pulse, heart sounds thin and flabby, giving one the idea of thin-walled, dilated cavities and of small muscular power." If the blood-pressure is low, it can be detected by the sphygmomanometer. A finding of a lymphocytosis or diminution of the hemoglobin of the blood would aid in the diagnosis. Inspection of the chest may possibly show a pulsating tumor above the sternum, when the thymus is greatly enlarged, or this tumor may be palpated by the finger of the examiner.

Percussion. Light percussion with the finger should be employed. Warthin says: "The area of thymic dullness is triangular, with unequal sides, the base at the level of the sterno-clavicular articulations, and the blunt apex is behind the second intercostal space or the upper part of the third rib. The side boundaries extend somewhat beyond the sternal lines, usually more to the left than to the right. An area of dullness extending more than one centimeter beyond the sternal lines may be taken as evidence of an enlarged thymus."

In a case of thymic asthma, during the attack, we have the picture of a child suffering from inspiratory dyspnea. The respiration is noisy and stridorous in character. There is retraction of the supra-clavicular and intercostal spaces. The child is very restless and perhaps cyanosed. No history of a diphtheritic infection is obtainable. Examination of the larynx is negative, but tracheal stenosis is demonstrable by a long tracheoscopic tube (Jackson).

The most certain and only reliable method of diagnosis is radiography. Warthin states "that the radiogram of the normal thorax of an infant shows in the median line a flask-shaped shadow having a narrow neck and plump body, the neck portion of the shadow reaching from the first or second dorsal vertebra to the fifth or sixth. The body of the flask corresponds to the cardiac shadow, while the neck shadow—the lateral boundaries of which only slightly exceed those of the vertebrae—is the shadow of the thymus and great vessels. Under pathological conditions, i. e., with hypertrophy of the thymus, the neck portion of the shadow broadens." Warthin has well shown this by radiograms.

Resume. 1. The thymus gland is probably an epithelial organ with an internal secretion.

2. The diagnosis of status lymphaticus as a cause of death is made too frequently. Hammar's statistics show that the thymus gland is normally much larger than is generally supposed.

3. Mechanical tracheo-stenosis undoubtedly exists as a cause of death in rare instances.

4. The usual cause of death in status lymphaticus is probably a "hyperthymization" of the organism, which renders it peculiarly susceptible to harmful external influences, such as shock, anesthetics and infectious disease.

5. The diagnosis of status lymphaticus can undoubtedly be made *intra vitam*. The X-ray offers the most certain and reliable means of determining the presence or absence of an enlarged thymus gland.

6. If status lymphaticus exists, chloroform is the most dangerous anesthetic.

The following is a list of some of the more important articles on the subject:

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